From: Sherman Hom
To: FLERCHINGER Margaret
Subject: Fwd: Request for advice
Date: Friday December 10 2021 10:47:35 AM
Attachments: Recommendation Letter for OR OMMP on Required Microbial Testing of Cannabis.pdf

Ms. Flerchinger
I have attached our letter that contains recommendations for modification of the proposed draft regulations that delineates the required microbial testing regimen.

If there is a person that should have gotten this letter, I would appreciate it very much if you could forward the letter to the appropriate person.

Lastly, I would like to share with you my cannabis testing and regulatory experience, which was mostly in state government.
In 2012 at the New Jersey Department of Health Public Health and Environmental Laboratories (PHEL), I was the Project Manager that led a team of chemists to start the first Cannabis Testing Lab in NJ. The team validated the quantitative determination of cannabinoids, metals, and mycotoxins.
In 2019-2021 at PHEL, I was the Project Manager for the validation of microbial testing of cannabis.
In 2017-2020 at PHEL, I was the Project Manager that led a team that created and maintained a compendium of the all states medical cannabis programs required testing of all analytes with their corresponding action levels. Comparative analyses were performed to identify trends and gaps in required testing rules.
In May 2021, I joined Medicinal Genomics Corporation as their Director of Regulatory Affairs. My primary responsibility is to have dialogues with persons at state regulatory bodies that are responsible for either drafting and/or modifying cannabis required testing regulations; especially testing for microbial contamination.

If you have any questions, please do not hesitate to reach out to me.

I thank you for your time and consideration.

Respectfully
Sherman

---------- Forwarded message ---------
From **Sherman Hom** <sherman hom@medicinalgenomics com>
Date Fri, Dec 10, 2021 at 11 19 AM
Subject Request for advice
To <Margaret FLERCHINGER@dhsoha state or us>

Ms. Flerchinger
I have written a letter that contains our recommendations for modifying the proposed draft rules that describe the required microbial testing of cannabis.

These proposed draft rules were found in the following link
https //www oregon gov/oha/PH/DISEASESCONDITIONS/CHRONICDISEASE/MEDICALMARIJUANAPROGRAM/Documents/rules/Summary%20of%20proposed%20testing%20requirement%20changes%2010-20-2021 pdf

I would appreciate it very much if you could tell me who I should address the letter to and what email address I should send the letter.

I thank you for your time and consideration.

Respectfully
Dr. Hom

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Director of Regulatory Affairs
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December 10, 2021

Margaret Flerchinger
Rules and Operations Liaison
Medical Marijuana Program
Oregon Public Health Division

Dear Ms. Flerchinger,
As industry leaders in cannabis and pathogen genomics, we have spent decades working with quantitative polymerase chain reaction (qPCR) and culture-based methods for the detection of microorganisms. We are experts in the field with over 40 patents related to PCR and DNA sequencing based methods for detecting microorganisms. Kevin McKernan, Chief Scientific Officer at Medicinal Genomics Corporation (MGC) managed the Research and Development team for the Human Genome Project at the Whitehead Institute of Massachusetts Institute of Technology. He has over 45,743 citations related to his work in this field. Our scientists recommend the microbial testing specifications that will ensure that cannabis manufactured products are safe for patients and consumers. Due to our concerns for public health, we feel that the Oregon Medical Marijuana Program should consider modifying the proposed draft rules (dated 10/20/21) [1] that describe the changes in required microbial testing of cannabis to reflect ongoing efforts at the AOAC, USP, CDC, and FDA, which are consistent with our findings at MGC.

The presence of microorganisms is common in natural products, such as cannabis flowers. One must be able to differentiate between harmless and/or beneficial microbes ubiquitous in nature and those that are human pathogens that have contaminated the cannabis plant and/or manufactured products. Examples of specific human pathogens that have been detected in cannabis are Shiga toxin producing *E. coli* (STEC), *Salmonella* spp. (all species are pathogenic), *Aspergillus flavus, A. fumigatus*, *A*. *niger*, and *A*. *terreus* [2-16].

Current required testing regimens for microbial contamination in states that have medical and adult-use cannabis programs vary among the states. Some states require a combination of some of the following tests: total yeast and mold count (TYM), total aerobic microbial count (TAMC), total coliform count, total bile-tolerant Gram-negative bacteria count (BTGN), total *E. coli,* STEC, *Salmonella* spp., and the 4 species of *Aspergillus* (see above). Action levels for each test and each cannabis product type are dependent on each state's regulations. All microbial tests have action levels as colony forming units (cfu/g), which is the number of colonies that grow on the surface of an agar medium plate. On the other hand, some states, such as California for inhalable cannabis and cannabis flowers require tests to detect STEC, *Salmonella* spp., *Aspergillus fumigatus*, *A*. *flavus*, *A*. *niger*, and *A*. *terreus* with an action level of none detected per gram of product. These states for non-inhalable cannabis products require tests to detect STEC and *Salmonella* spp.

In the proposed draft Cannabis Testing Requirements (OAR 333-007-0320 Compliance Testing Requirements, it states that 1) Marijuana/Usable marijuana, 2) Finished Extract/ Concentrate, 3)

Finished Inhalable Cannabinoid Product, and 4) Hemp-Derived Vapor Items that is either intended for sale from a dispensary or further processing into a product must be tested for the following microorganisms:

a. Total yeast and mold
b. Aspergillus flavus
c. Aspergillus fumigatus
d. Aspergillus niger
e. Aspergillus terreus

NOTE: No action levels were delineated for each microbial test and/or sample type.

Our first concern is that total microbial count tests ("indicator tests") like Total Yeast and Mold **do not** test directly for the presence of any specific human pathogens. The American Herbal Pharmacopoeia's *Cannabis* Inflorescence *Cannabis* spp. monograph [17] states that total microbial counts **must never** be used to pass or fail a cannabis sample. Total count results **do not** provide any information about the presence of any pathogenic microorganisms in the cannabis sample, which may cause harm to patients and consumers.

Our second concern is that additional human pathogens that have been detected in cannabis, such as *Salmonella* spp. and shiga toxin producing *E. coli* should also be included in the required testing regimen.

Therefore, Medicinal Genomics **recommends** that the Medical Marijuana Program consider microbial testing rules to include required microbial testing for medical and adult-use cannabis and cannabis products to include the pathogen specific tests. For inhalable cannabis and cannabis products, we recommend the six tests, which are

1. *Salmonella* species
2. Shiga-toxin producing *Escherichia coli* (STEC)
3. *Aspergillus flavus*
4. *Aspergillus fumigatus*
5. *Aspergillus niger*
6. *Aspergillus terreus*

On the other hand for non-inhalable products, we recommend tests 1 and 2 listed above.

Since these microorganisms are dangerous to human health, the action levels for all six tests should be "None detected/gram". Fourteen (14) states (AK, AZ, CA, CO, FL, HI, IA, MI, MO, MT, OK, NV, SD, and VT) have either required the tests to detect the human pathogens listed above or have drafted regulations to add to or replace Total Count tests with the tests to detect human pathogens.

Medicinal Genomics also recommends that the the required microbial testing for medical and adult-use cannabis and cannabis products rules should include a statement concerning allowable methods to read:

1. A validated method using guidelines for food and environmental testing put forth by the USP, FDA, and AOAC Appendix J and cannabis as a sample type; or

2. Another approved AOAC, FDA, or USP validated method using cannabis as a sample type."

NOTE: "Another approved AOAC, FDA, or USP validated method using cannabis as a sample type" may include molecular methods, such as qPCR."

The reasons for this recommendation are outlined below.

Currently there are limited AOAC, FDA, or USP approved species specific pathogen testing methods for cannabis. Medicinal Genomics released the first version of our SenSATIVAx® (DNA extraction) and PathoSEEK® (qPCR assay) Manufacturer Validation Document in 2017. These method validations use cannabis as the sample type. At that time, there were no official guidelines published by any regulatory body describing how to validate a method for detecting microbes in the presence of a cannabis matrix. Due to this lack of available guidelines in the cannabis industry, our scientific team referenced guidelines for food and environmental testing put forth by the USP, FDA, and AOAC Appendix J. We continually add data to this document as we release new assays or make improvements to current assays. We are currently on version 31 of this document [18]. In addition, MGC's methods are currently going through additional validation according to AOAC's Standard Method Performance Requirements (SMPRs). AOAC has released 3 SMPRs for species specific testing for the species specific pathogens listed above (see #1-3 below).

1. Detection of *Aspergillus* in Cannabis and Cannabis Products https://www.aoac.org/wp-content/uploads/2019/10/SMPR-2019_001.pdf
2. Detection of *Salmonella* species in Cannabis and Cannabis Products https://www.aoac.org/wp-content/uploads/2020/07/SMPR-2020_002.pdf
3. Detection of Shiga toxin-producing *Escherihia coli* in Cannabis and Cannabis Products https://www.aoac.org/wp-content/uploads/2021/02/SMPR-2020_012.pdf

Medicinal Genomics is a member of **AOAC's Cannabis Analytical Science Program (CASP) Microbial Contaminants Working Group**. The goal and objectives of this working group are to

- Develop Standard Method Performance Requirements (SMPR) for cannabis and hemp
- Extend a Call for Methods for each of the completed SMPRs
- Empanel an Expert Review Panel to review candidate methods
- Deliver consensus-based validated Performance Test Methods (PTMs) & Final Action Official Methods for the cannabis industry

NOTE: Medicinal Genomics has an AOAC Certified qPCR PTM for the detection of the 4 *Aspergillus* species, which was approved on August 10, 2021 and will have an AOAC Certified qPCR PTM for the detection of *Salmonella* spp. & STEC by January 2021. The sample types for both tests are/will be cannabis flower and infused products.

The primary advantage of using qPCR detection assays are that they are designed to identify unique specific DNA sequences either shared by a "group" of bacteria, such as all *Salmonella* species and STEC strains or a specific genus and specie, such as the 4 different pathogenic *Aspergillus* species. If the unique sequences are present, then the qPCR test will detect it. Therefore, a qPCR test is very specific, very sensitive, and possesses a rapid turnaround time (6 hours) *vs.* plating methods that are less specific,

less sensitive, and has a very slow turnaround time of days for colonies to form on a plate. Moreover, MGC has developed a method to remove the DNA from dead cells by using a DNA nuclease enzyme, incubation, & nuclease inactivation step before amplification to detect any DNA from live pathogens [19].

Furthermore, there are additional major disadvantages of using plating methods to detect species specific bacterial and fungal pathogens.

- The cannabinoids, which represent 10-20% of the cannabis flower by weight, have been shown to have antibiotic activity. Antibiotics inhibit the growth of bacteria in plating methods. *Salmonella* and STEC bacteria are very sensitive to antibiotics, which may lead to a false negative result.
- Plating methods cannot detect endophytes, which are molds that live a part or all of their life cycle inside a plant. Examples of endophytes are the species specific *Aspergillus* pathogens and *Fusarium*. Methods to break open the plant cells to access these endophytes for plating methods also lyses these mold cells (killing these cells in the process). Therefore, these endophytes will not be able to form colonies in a plating method.
- Selective media for mold plating methods, such as Dichloran Rose-Bengal Chloramphenicol (DRBC) reduces mold growth; especially *Aspergillus* by 5-fold. This may lead to a false negative result for this human pathogen. In other words, although DRBC medium is typically used to reduce bacteria; it comes at the cost of missing 5 fold more yeast and molds than Potato Dextrose Agar (PDA) + Chloramphenicol or molecular methods. These observations were derived from study results of the AOAC emergency response validation [20].

Respectfully,

Sherman Hom, Ph.D.

Director of Regulatory Affairs
Medicinal Genomics

References

1. Summary of Proposed Cannabis Testing Changes, DRAFT, 10/20/2021, OAR 333-007-0320 Compliance Testing Requirements for Marijuana or Usable Marijuana, https://www.oregon.gov/oha/PH/DISEASESCONDITIONS/CHRONICDISEASE/MEDICALMARIJUANAPROGRAM/Documents/rules/Summary%20of%20proposed%20testing%20requirement%20changes%2010-20-2021.pdf
2. M.J. Chusid, J.A. Gelfand, C. Nutter, and A.S. Fauci, *Ann. Intern. Med.* 82(5), 61–64 (1975).
3. R. Llamas, D.R. Hart, and N.S. Schneider, *Chest* 73(6), 871–2 (1978).
4. S. Sutton, B.L.Lum, and F.M. Torti, *Drug Intell. & Clin. Pharm.* 20(4), 289–291 (1986).
5. R. Hamadeh, A. Ardehali, R.M. Locksley, and M.K. York, *Chest* 94(2), 432–33 (1988).
6. D.W. Denning, S.E. Follansbee, M. Scolaro, S. Norris, H. Edelstein, and D.A. Stevens, *N. Engl. J. Med.* 324(10), 652–664 (1991).
7. W.H. Marks, L. Florence, J. Lieberman, P. Chapman, D. Howard, and P. Roberts, et. al., *Transplant* 61(12), 1771–1774 (1996).
8. M. Szyper-Kravitz, R. Lang, Y. Manor, and M. Lahav, *Leukemia & Lymphoma* 42(6), 1433–1437 (2001).
9. R. Ruchlemer, M. Amit-Kohn, and D. Raveh, et. al., *Support Care Cancer* 23(3), 819–822 (2015).
10. D.W. Cescon, A.V. Page, S. Richardson, M.J. Moore, S. Boerner, and W.L. Gold, *J. Clin. Oncol.* 26(13), 2214–2215 (2008).
11. A. Bal, A.N. Agarwal, A. Das, S. Vikas, and S.C. Varma, *Pathol.* 42(2), 197–200 (2010).
12. Y. Gargani, P. Bishop, and D.W. Denning, *Mediter. J. Hematol. Infect. Dis.* 3:e2011005 Open Journal System (2011).
13. S.L. Kagen, M.D. Viswanath, P. Kurup, P.G. Sohnie, and J.N. Fink, *J. Alleg. Clin. Immunol.* 71(4), 389–394 (1983).
14. D.N. Taylor, I.K. Wachsmuth, Y.H. Shangkuan, E.V. Schmidt, T.J. Barrett, and J.S. Schrader, et. al., *NEJM* 306(21), 1249–1253 (1982).
15. S.L. Kagen, *NEJM* 304(8), 483–484 (1981).
16. J.L. Pauly and G. Paszkiewicz, *J. Oncol.* 2011: 819129 (2011).
17. American Herbal Pharmacopoeia's *Cannabis* Inflorescence *Cannabis* spp. Monograph https://herbal-ahp.org/online-ordering-cannabis-inflorescence-qc-monograph/
18. MGC Validation Document https://1280717.app.netsuite.com/core/media/media.nl?id=5910362&c=1280717&h=6e4d1cce15d1eae41733&_xt=.pdf&fcts=20191014094610&whence=
19. Solving qPCR's Live-Dead Problem https://www.medicinalgenomics.com/solving-the-live-dead-problem/
20. Whole genome sequencing of colonies derived from cannabis flowers & the impact of media selection on benchmarking total yeast & mold detection tools: https://f1000research.com/articles/10-624